betaDiketonate-Iron(III) Complex: A Versatile Fluorine-19 MRI Signal Enhancement Agent.

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Public Summary:
Fluorine-19 magnetic resonance imaging (MRI) has gained considerable momentum as a promising imaging modality for in vivo tracking of cellular therapies and as a diagnostic for inflammatory disease. To further the utility of this technique, we increase imaging probe sensitivity by merging paramagnetic metal chelates with aqueous perfluorocarbon (PFC) nanoemulsions. We prepared a highly fluorinated ferric tris(β-diketonate) chelate (MW = 1265.2 g/mol) at gram scale. This iron chelate is soluble in multiple PFC oils used for MRI and readily reduces the 19F longitudinal relaxation time (T1) to <100 ms with modest line broadening and displays superior properties for 19F MRI applications. The sensitivity enhancement by Fe(III) laden PFC nanoemulsion was confirmed in MRI phantom studies, where reduced T1 speeds data acquisition thereby increasing the 19F image sensitivity per time via signal averaging. Additionally, 19F relaxivity of nanoemulsions incorporating other metal ions, including Gd, Er, Ho, Dy, Mn, Cr, and Ni, were evaluated. High-moment lanthanide ions, such as Gd(III), display severe line broadening, but other ions [e.g., Ho(III)] induce pseudocontact chemical shifts (up to 0.5 ppm) of 19F in nanoemulsion, which makes them potentially useful for multichromatic 19F imaging. Formulated nanoemulsions have a shelf life >200 days. Free β-diketonate or its iron complex in formed PFC nanoemulsion did not induce cytotoxicity in intracellularly labeled macrophages. Overall, ferric tris(β-diketonate) chelate provides a scalable approach for boosting sensitivity of PFC-based 19F MRI probes. More generally, it can functionalize PFC oil, whose chemical modification remains challenging.

Scientific Abstract:
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